The ideal system for testing the NBS method for its capabilities under favorable (but not uncommon) circumstances would be with a protein which contained only one of the susceptible amino acids. This is the case for rabbit thymus lysine-rich histone (mol wt 21,000), which contains a single tyrosyl residue, but no tryptophan, histidine, or sulfur-containing amino acids.[3] As reported previously,[4] NBS cleaves the lysine-rich histone at its single tyrosyl residue, producing two components which are separable on Sephadex G-100. The yields of the two components (N_1 and N_2) were not quantitative and they were unequal on a molar basis, and therefore it seemed that the cleavage was similar to that in more complicated proteins. Now, however, we are able to recover both fragments in nearly quantitative yields (Table I).

Table I. Representative Yields of NBS Fragments of Rabbit Thymus Lysine-Rich Histone

Applied with sucrose Yield, %		Applied without sucrose Yield, %	
N_1	N_2	N_1	N_2
44[a]	91[a]	99	91
49	84	97[a]	97[a]

[a] Yields calculated for Figure 1.

The large discrepancy in the yields of the two fragments which was observed previously can be eliminated by omitting sucrose from the sample applied to the G-100 column. The dramatic effect this has on yield and chromatographic pattern can be seen in Table I and Figure 1.

The manufacturer (Pharmacia Fine Chemicals, Inc.) recommends that application of samples to columns of Sephadex G-100 be accomplished with the aid of an inert substance such as sucrose so that the sample may be applied as a dense solution beneath a layer of eluent, thus facilitating the application and preventing disturbance of the resin. The use of sucrose, however, has an unsatisfactory effect on the chromatography of fraction N_1, which is highly basic.[3,4]

When the products of NBS cleavage are chromatographed with sucrose included in the application mixture, fraction N_1 shows a large tail which underlies the peak containing the other peptide fraction (N_2). If the amount of N_1 recovered is calculated just from the symmetrical portion of the first peak, its yield is very much less than that of N_2. When the area under the tailing portion of the chromatogram is summed with N_1, the yields of N_1 and N_2 become very nearly equal. Amino acid analysis of the tailing portion has confirmed that these regions are largely N_1. The reason for this effect of sucrose is as yet unexplained, although it may be related to the high lysine content of N_1 and the acidic solvent used for chromatography. Perhaps a weak reversible three-way binding of peptide–sucrose–Sephadex occurs causing transient retention of the peptide and dissociation occurs progressively as the peptide and sucrose are gradually separated on the column. In any case when sucrose is not used both peaks are symmetrical and give nearly quantitative yields.

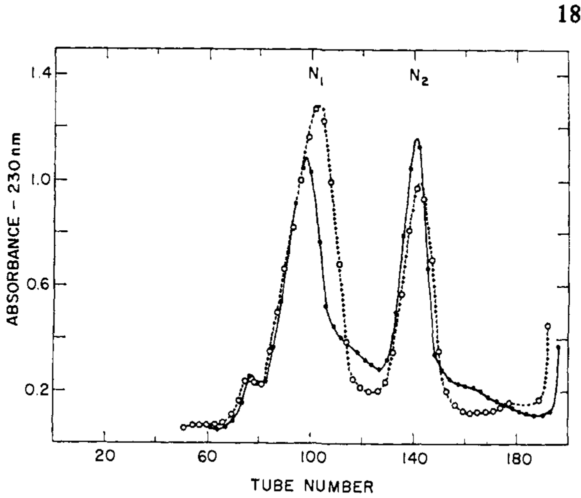

Figure 1. Chromatography of the NBS reaction mixture of a rabbit thymus lysine-rich histone on a column (2 × 190 cm) of Sephadex G-100 (particle size 40–120 μ). In each case 3.3×10^{-6} mol of starting material was treated with NBS, applied to the column, and eluted with 0.02 *N* HCl at 3 ml per tube. Yields when applied with sucrose: tubes 85–110, 44%; tubes 129–152, 91%. Yields when applied without sucrose: tubes 85–117, 97%; tubes 129–153, 97%: —●—, absorbance when applied with sucrose; --○--, absorbance when applied without sucrose.

The nearly quantitative cleavage of tyrosine by NBS in lysine-rich histone points out how useful this method can be when applied to proteins or peptides which contain only one of the residues susceptible to NBS oxidation. Thus, NBS offers an excellent alternative to enzymatic or other chemical methods, such as cyanogen bromide, for structural studies on peptides and proteins.

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Neighboring Boron in a Concerted Electrophilic Displacement

Sir:

Direct bonding interaction between the attacking and leaving groups has been postulated to be a general feature of electrophilic displacements with retention at tetrahedral carbon.[1,2] The methyl-bridged aluminum compound $Al_2Me_5NPh_2$ (**1**), which has been characterized by X-ray diffraction,[3] is a reasonable model for the transition state (**2**) of a typical electrophilic displacement, mercurideboronation.[2a,4]

It is difficult to obtain experimental evidence for the three-center electron-pair bond (represented by the dashed-line triangle) and the boron–oxygen–mercury

(1) S. Winstein, T. G. Traylor, and C. S. Garner, *J. Amer. Chem. Soc.*, 77, 3741 (1955).

(2) Reviews: (a) D. S. Matteson, *Organometal. Chem. Rev.*, *A*, **4**, 263 (1969); (b) F. R. Jensen and B. Rickborn, "Electrophilic Substitution of Organomercurials," McGraw-Hill Book Co., New York, N. Y., 1968; (c) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965.

(3) V. R. Magnuson and G. D. Stucky, *J. Amer. Chem. Soc.*, **91**, 2544, (1969).

(4) D. S. Matteson and E. Krämer, *ibid.*, **90**, 7261 (1968).

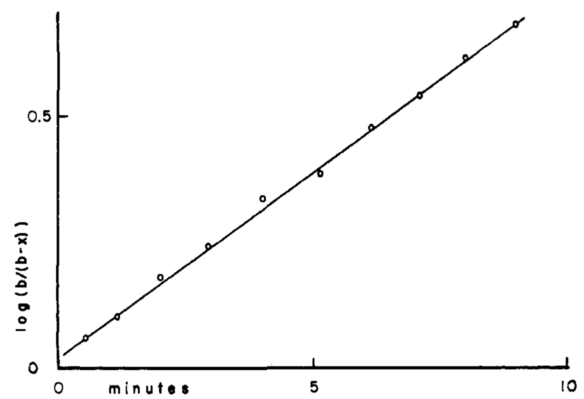
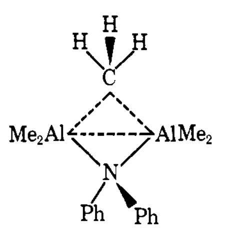
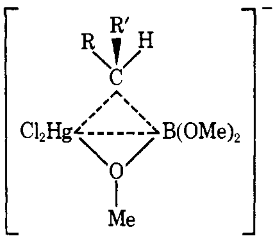


Figure 1. Plot of log [$b/(b-x)$] *vs.* time for reaction of $CH_2[B(OMe)_2]_2$ with $HgCl_2$, where b is $[HgCl_2]_0$ and x is the amount reacted.

linkage in the transition state (**2**), since there is no system for comparison in which these interactions are known to be absent.



1 (stable)



2 (transition state)

Neighboring group effects may provide a way around this impasse. We have measured rates of reaction of substituted methaneboronic esters with mercuric chloride in buffered methanol.

$$ZCH_2B(OMe)_2 + HgCl_2 + OAc^- + MeOH \longrightarrow ZCH_2HgCl + B(OMe)_3 + HOAc + Cl^-$$

The results, summarized in Table I, are consistent with transition state structure **2**.

Table I. Rates of Reaction with $HgCl_2$ at 30° and pK_a's in Methanol

Compd	pK_a	k, l./mol sec	k/k_0 per boron
$CH_3B(OMe)_2$	10.6	6.7×10^{-4}	1.0
$CH_2[B(OMe)_2]_2$	10.8	0.131	98
$ClHgCH_2B(OMe)_2$[a]	[b]	2.0×10^{-3}	3.0
$C_6H_5CH_2B(OMe)_2$	9.7	2.4×10^{-4}	0.36
$HC[B(OMe)_2]_3$	[b]	~0.27[c]	~135
$C[B(OMe)_2]_4$	[b]	~0.016[c]	~6

[a] We have isolated $ClHgCH_2B(OMe)_2$, $ClHgCH_2B(OH)_2$, and $CH_2(HgCl)_2$ and will report the details later. [b] Side reactions with base preclude pK measurements. [c] Some erratic results were obtained and the number of borons replaced is not known.

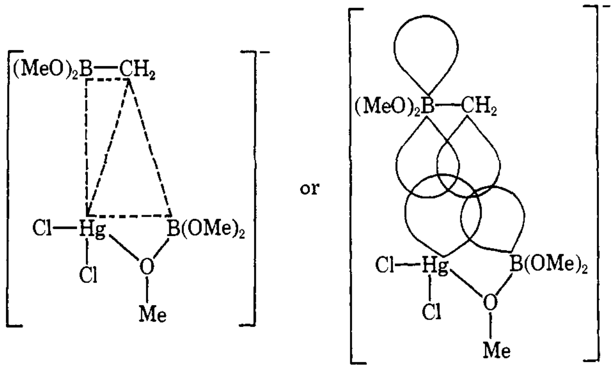
The rapid reaction of bis(dimethoxyboryl)methane, $CH_2[B(OMe)_2]_2$,[5] with mercuric chloride is not quenched by EDTA, and therefore our previous analytical method[4] failed. Instead, 1-ml aliquots were mixed with dithizone solution (3.8 ml, 3×10^{-4} *M* in carbon tetrachloride), then shaken at once with 100 ml of water to remove sodium acetate, which interferes. Two molecules of dithizone per $HgCl_2$ and one per RHgCl are complexed. The free dithizone was estimated spectrophotometrically at 625 nm. Fifteen runs were made with mercuric chloride initially 10^{-3} *M* and with eightfold variation of each of the other reagents: $CH_2[B(OMe)_2]_2$, sodium acetate, acetic acid, and sodium chloride (which represses ionization of $HgCl_2$). The rate law is

$$-d[HgCl_2]/dt = k[RB(OMe)_2][HgCl_2][NaOAc]/[HOAc]$$

The observed k is 0.169 (±0.019, maximum deviation 0.039) l./mol sec. A typical pseudo-first-order plot is shown in Figure 1.

Equal concentrations of mercuric chloride and $ClHgCH_2B(OMe)_2$, which complexes with dithizone, are preferred for kinetic measurements. The k values in Table I were obtained from second-order plots with $[HgCl_2]_0 = [RB(OMe)_2]_0 = 0.004$ *M* (except $CH_3B(OMe)_2$ and $PhCH_2B(OMe)_2$ were 0.04 *M*), [NaOAc] = 0.06 *M*, [HOAc] = 0.025 *M*, and [NaCl] = 0.05 *M*.

The high reactivity of $CH_2[B(OMe)_2]_2$ is in accord with transition state model **2**. The vacant p orbital of the stationary boron atom can overlap with the carbon and mercury σ orbitals to expand the three-center electron-pair bond to four centers and thus lower the energy (structure **3**). (There may also be a weak Hg–Cl–B ligand bridge.) The mercury atom in $ClHgCH_2B(OMe)_2$ likewise furnishes a vacant p orbital, but it bonds weakly and accelerates the reaction only moderately (Table I). The phenyl group retards the reaction of $C_6H_5CH_2B(OMe)_2$ because it has no vacant bonding orbital.



3

A brief study of temperature dependence yielded $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values consistent with transition states **2** and **3**. For $CH_2[B(OMe)_2]_2$, $\Delta H^{\ddagger} = 8.8$ (±1.5) kcal/mol and $\Delta S^{\ddagger} = -33$ eu (from $k = 0.032$ at 0.3°, 0.088 at 20°, 0.137 at 30°, and 0.278 at 40°). For $CH_3B(OMe)_2$, $\Delta H^{\ddagger} = 15.4$ and $\Delta S^{\ddagger} = -22$ (from $k = 2.85 \times 10^{-4}$ at 20°, 6.7×10^{-4} at 30°, and 1.64×10^{-3} at 40°). For $C_6H_5CH_2B(OMe)_2$, $\Delta H^{\ddagger} \cong 16.2$ and $\Delta S^{\ddagger} \cong -21$.

Are our results consistent with a transition state model (**4**) which lacks metal–metal bonding and ligand bridging? Boron can stabilize carbanions,[5,6] but our rate law rules out any free carbanion intermediate. Observations inconsistent with carbanion character in the transition state include lack of correlation of rates

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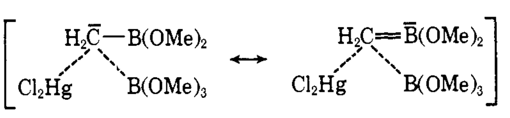
(5) R. B. Castle and D. S. Matteson, *J. Amer. Chem. Soc.*, **90**, 2194 (1968); *J. Organometal Chem.*, **20**, 19 (1969).

(6) For example: G. Zweifel and H. Arzoumanian, *J. Amer. Chem. Soc.*, **89**, 291 (1967).



4 (unlikely)

with pK_a's (Table I), the $\Delta S^{\ddagger}$ values, a previous Hammett correlation of ArCH$_2$B(OR)$_2$ reaction rates,[4] failure of HC[B(OMe)$_2$]$_3$ and C[B(OMe)$_2$]$_4$ to show greatly enhanced reactivity over CH$_2$[B(OMe)$_2$]$_2$ as observed in carbanion reactions,[5,7] and failure of 10% water or 0.04 *M* sodium nitrate to accelerate measurably the reaction of CH$_2$[B(OMe)$_2$]$_2$. Nonpolar stabilization of loosened bonding by π delocalization ought to parallel radical stabilization, for which B(OR)$_2$ is less effective than phenyl.[8]

Previous observations which might be reinterpreted on the basis of transition states analogous to **3** include electrophilic cleavages of Me$_3$SiCH$_2$ from (MeSiCH$_2$)$_2$SnR$_2$[9] and the unusual mercuration of acetic acid, which appears to be facilitated by the carboxyl group without involving an enol.[10]

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(7) (a) D. S. Matteson and G. L. Larson, *J. Amer. Chem. Soc.*, **91**, 6541 (1969); (b)D. S. Matteson and J. R. Thomas, to be published.

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(9) D. Seyferth, *ibid.*, **79**, 5881 (1957).

(10) W. Kitching and P. R. Wells, *Aust. J. Chem.*, **18**, 305 (1965).

(11) (a) We thank the National Science Foundation for support, Grant No. GP-9320; (b) Alfred P. Sloan Foundation Fellow, 1966–1968.

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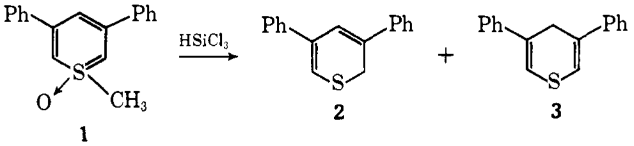
Thiabenzenes. II. Generation and Ylidic Properties of 1-Methyl-3,5-diphenylthiabenzene

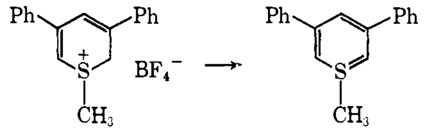
Sir:

Current interest in the type of bonding dominant in "tetravalent sulfur" heterocycles,[1] in thiabenzenes,[2–4] and in other thiacyclic systems[5] has led us to investigate the possibility of converting thiabenzene 1-oxides[4] into 1,3,5-trisubstituted thiabenzenes. We wish to describe a synthesis of the title compound **5** *via* a novel reductive procedure, and to report some spectral and chemical properties of **5** which are consistent with an ylide-type bonding description for thiabenzenes.



1 **2** **3**

Treatment of 1-methyl-3,5-diphenylthiabenzene 1-oxide (**1**)[4,6] with 1 mol equiv of trichlorosilane[7] in refluxing benzene (9 hr) afforded a 3:2 mixture of 2*H*- and 4*H*-3,5-diphenylthiopyrans, **2** and **3** (77% yield),[8] from which the 2*H* isomer **2** could be isolated by chromatography (Florisil) followed by recrystallization (EtOH): mp 104.6–106.1°; uv max (EtOH) 270 (ε 30,600) and 364 nm (ε 4900); nmr (CCl$_4$) δ 3.60 (t, 2, *J* ~ 0.6–0.9 Hz), 6.40 (q, 1, *J* ~ 0.6 Hz), 6.54 (q, 1, *J* ~ 0.9 Hz), and 7.2–7.8 (m, 10).[9] Reaction of **2** with methyl iodide–AgBF$_4$[10] gave 1-methyl-3,5-diphenyl-2*H*-thiinium tetrafluoroborate (**4**): mp 144.5–145.3° dec; uv max (EtOH–H$_2$O [2:1]) 244 (ε 32,300), 291 (ε 15,600), and 331 nm (ε 11,300); nmr (DMSO-d_6) δ 2.97 (s, 3), 4.78 (d, 2, *J* ~ 1.0 Hz), 6.78 (d, 1, *J* ~ 0.7 Hz), 7.28 (q, 1, *J* ~ 0.9 Hz), and 7.37–7.97 (m, 10).[9]



4 **5**

Treatment of **4** with base under a variety of conditions effected the generation of 1-methyl-3,5-diphenylthiabenzene (**5**). In a typical experiment, 1.24 *M* *t*-butyllithium (0.24 mmol) in pentane was added to a solution of 85 mg (0.24 mmol) of **4** in 0.30 ml of DMSO-d_6 under N$_2$ in a standard nmr tube and the two layers were mixed yielding an orange solution which showed nmr peaks attributable to **5** at δ 1.73 (s, *2.5*), 4.03 (d, 2, *J* = 1.7 Hz), 6.18 (t, 1, *J* = 1.7 Hz), and 7.21–7.82 (m, 10);[11] an increase in area at δ 2.50 corresponding to ~1.7 protons as DMSO-d_x was also noted, indicating that, in addition to removal of one proton at C-2 in **4** by methylsulfinylcarbanion-d_5 (from DMSO-d_6 and *t*-butyllithium), additional base-catalyzed exchange of the S-methyl protons of **5** had occurred before complete mixing (and reaction) of **4** with the anion had taken place.[12] Addition of aqueous HBF$_4$ (0.24 mmol) to the solution of **5** after 1.0 hr at 35° (during which time little decomposition of **5** had occurred) led to regeneration of **4** (nmr). Treatment of the solution with water and petroleum ether yielded 39 mg (46% recovery) of **4**, obtained by slow crystallization from the aqueous layer; mp 142.6–143.9° dec; nmr (DMSO-d_6) δ 2.97 (*2.5*), 4.78 (2), 6.77 (1), 7.23 (1), and 7.40–7.97 (10); the petroleum ether layer gave 16 mg of orange oil which showed only broad absorption (nmr) in the phenyl-H region.

Thiabenzene **5** could also be generated by treatment of a degassed ethanolic solution of **4** with oxygen- and carbonate-free aqueous NaOH at room temperature and exhibited uv max (0.02 *N* NaOH in EtOH–H$_2$O (4:1)) at 245 (ε 33,700), 275 (ε 14,300 [sh]), and 437 nm

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(1) I. S. Ponticello and R. H. Schlessinger, *Chem. Commun.*, 1214 (1969); M. P. Cava and G. E. M. Husbands, *J. Amer. Chem. Soc.*, **91**, 3952 (1969).

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(5) W. G. Salmond, *Quart. Rev.* (London), **22**, 253 (1968).

(6) T. M. Harris, C. M. Harris, and J. C. Cleary, *Tetrahedron Lett.*, 1427 (1968).

(7) Trichlorosilane has been reported to convert phosphine oxides to phosphines (with inversion of configuration): L. Horner and W. D. Balzer, *ibid.*, 1157 (1965).

(8) Since the completion of this work, reports have appeared on the use of HSiCl$_3$ in the reduction of sulfoxides to sulfides (T. H. Chan, A. Melnyk, and D. N. Harpp, *ibid.*, 201 (1969)), and on the use of Si$_2$Cl$_6$ and Si$_3$Cl$_8$ for the deoxygenation of phosphine oxides, sulfoxides, and amine oxides (K. Naumann, G. Zon, and K. Mislow, *J. Amer. Chem. Soc.*, **91**, 2788 (1969)).

(9) Satisfactory analyses for C, H, S, and F were obtained. Melting points were determined in evacuated capillary tubes and are corrected.

(10) T. E. Young and R. Lazarus, *J. Org. Chem.*, **33**, 3770 (1968).

(11) Peaks due to pentane, dissolved 2-methylpropane, and other aliphatic substances in the *t*-butyllithium solution are not listed; no other peaks (except that for DMSO-d_x) were observed.

(12) This interpretation is supported by the integrated area of the S-methyl peak at δ 1.73 which corresponded to 2.5 protons, and the further observation that, in other experiments, this area was dependent on the mode of mixing and varied over a range corresponding to 0–3 (±10%) S-methyl protons in **5**. Base-catalyzed exchange of S-methyl protons has also been observed for **1**.[4]